

subjecting said mutant hippocampal cells to tetanic stimulation; and

determining the effect of said candidate drug on the synaptic potentiation of said mutant hippocampal cells[;], wherein a reduction in [the] said enhanced synaptic potentiation of said mutant hippocampal cells is indicative of the activity of a candidate drug efficacious for the treatment of Alzheimer's disease.

2. (Amended) [A] The method according to Claim 1, wherein said mutant hippocampal cells are mutated in a presenilin gene.
3. (Amended) [A] The method according to Claim 2, wherein said mutant hippocampal cells are located in mouse hippocampal tissue slices
4. (Amended) [A] The method according to Claim 1, wherein said enhanced synaptic potential is as a result of change in [the] a GABA_A receptor mediated pathway.
5. (Twice amended) A method for screening for drugs for the treatment of Alzheimers's disease said method comprising:

contacting with a candidate drug mutant hippocampal cells having enhanced synaptic potentiation [stimulation as compared to wild-type hippocampal cells] upon tetanic stimulation comparable to that of hippocampal cells with a PS-1 mutation [with a candidate drug];

subjecting said mutant hippocampal cells to tetanic stimulation; and

measuring changes in potentiation with time of the mutant [and wild type] hippocampal cells in response to said candidate drug [and

comparing the effect of said agent on the synaptic potentiation of said mutant as compared to the observed synaptic potentiation of said wild type hippocampal cells;], wherein a reduction in [the] said enhanced synaptic potentiation of [the] said mutant hippocampal cells in response to tetanic stimulation [as compared to synaptic potentiation of the wild-type cells] is indicative of activity of a candidate drug efficacious for the treatment of Alzheimer's disease.

6. (Twice amended) A method for determining whether a mutation in hippocampal cells acts on a common pathway with a GABA_A receptor antagonist, said method comprising: [according to Claim 5, including the additional steps of]

contacting with a GABA_A receptor antagonist mutant hippocampal cells having enhanced synaptic potentiation upon tetanic stimulation [as compared to wild-type cells with a GABA_A receptor antagonist] comparable to that of hippocampal cells with a PS-1 mutation;

subjecting said mutant [and wild-type] hippocampal cells to tetanic stimulation
and

[measuring] determining changes in synaptic potentiation with time of [the] said mutant [and wild-type] hippocampal cells [and comparing the effects of said GABA_A receptor antagonist on said mutant [and said wild-type] hippocampal cells];, wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells treated with a GABA_A receptor antagonist [without a statistically significant change in the synaptic potentiation of the wild-type cells] is indicative of the mutation acting on a common pathway with said GABA_A receptor antagonist.

Cancel Claim 7.

8. (Twice amended) A method for screening for drugs for the treatment of Alzheimer's disease said method comprising:

contacting with a candidate drug wild type hippocampal cells and mutant hippocampal cells having enhanced synaptic potentiation upon tetanic stimulation comparable to that of hippocampal cells with a PS-1 mutation [as compared to wild-type hippocampal cells with a candidate drug];

subjecting said [mutant and] wild-type hippocampal cells and said mutant hippocampal cells to a tetanic stimulus at a first potential of glutamate currents and a second potential of GABA_A currents; and

measuring the synaptic response at each of the first and second potentials for the mutant and wild-type hippocampal cells and comparing the effect of the [agent] candidate drug on said mutant and said wild-type hippocampal cells[;], wherein a reduction in the enhanced synaptic response of the mutant hippocampal cells without a [statistically] significant change (p<0.5) in the synaptic response of the wild-type cells is indicative of activity of a candidate drug

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efficacious for the treatment of Alzheimer's disease.

9. (Twice amended) A method for screening for drugs for the treatment of Alzheimer's disease said method comprising:

contacting mutant mouse hippocampal cells mutated in the presenilin-1 gene and having enhanced synaptic potentiation upon tetanic stimulation as compared to wild type hippocampal cells with a candidate drug;

subjecting said mutant and wild-type hippocampal cells to tetanic stimulation;
and

comparing the effect of said [agent] candidate drug on said mutant and said wild-type hippocampal cells upon tetanic stimulation[;], wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells without a statistically significant change ($p < 0.5$) in the synaptic potentiation of the wild-type cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

10. (Amended) [Slices of mouse] Mouse hippocampal cells having a mutation in a presenilin gene combined with a candidate drug which inhibits the enhanced synaptic response of said cells to tetani.

11. (Amended) [Slices of mouse] Mouse hippocampal cells according to Claim 10, after tetanic stimulation.

12. (Amended) [Slices of mouse] Mouse hippocampal cells according to Claim 10, wherein said mutation is [the] a PS-1 delta 9 mutation.

REMARKS

The Claimed Invention

The claimed invention is directed to a method of screening candidate drugs for treating